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COMPLETE SPECIFICATION

NO DRAWINGS

Pharmaceutical Compositions Containing a Cresol or a Mixture of Cresols

I, ARISTOTELIS PAPAGEORGIOU-LAMBOS of 4 Monis Dohiariou Street, Athens, Greece, a Greek subject, do hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which is is to be performed, to be particularly described in and by the following statement:

This invention relates to novel pharmaceutical compositions useful in the treatment of certain conditions caused by pathogenic micro organisms, viruses, cocci microbes, and parasites and also in the treatment of fungi and allergies.

The cresols (*o* - cresol, *m* - cresol and *p* - cresol) are known to have anti-bacterial properties (cf Martindales Extra Pharmacoprica, 24th Edition, Volume 1, page 1017) but their use for this purpose has been limited in practice. I have now discovered that when the cresols are used in conjunction with strontium chloride ($SrCl_2$) as will hereinafter be more fully described the anti-bacterial and anti-microbial properties of the cresols are enhanced. It is an object of the present invention to provide a novel pharmaceutical composition containing a cresol or a mixture of cresols and strontium chloride, which composition has synergistic properties and is useful as an anti-bacterial agent in the treatment of certain conditions.

Thus, in accordance with the invention, there is provided a pharmaceutical composition for external and internal use comprising strontium chloride and one or more of *o*-cresol, *m*-cresol and *p*-cresol, and a pharmaceutically acceptable carrier therefor.

[Price 4s. 6d.]

Laboratory and clinical tests have shown that the anti-bacterial and anti-microbial properties of the novel compositions in accordance with the invention are considerably enhanced compared with those possessed either by any of the cresols alone or by any admixture of the cresols. Further the compositions of the invention are effective in the prevention of inflammations.

The quantities of the two active ingredients, i.e. the cresol, or mixture of cresols and the strontium chloride, in the composition will depend, as will be clearer hereinafter, on the intended use of the composition and method of application in any given case, but in most cases the composition will contain between 6 and 20% by weight strontium chloride and between 1 and 6% by weight of the cresol or cresols.

The method of preparing the compositions in accordance with the invention preferably comprises forming an aqueous solution (using distilled water) of the two active ingredients by conventional dissolution techniques followed by filtration of the solution. For some purposes the solution may be used as such, or in other cases further conventional pharmaceutically acceptable carriers, e.g. lanolin may be added to the solution to produce, for example, pastes, creams and ointments.

Examples of typical compositions in accordance with the invention for administration by the route indicated are as follows. (the percentages given for the active ingredients are by weight based on the total weight of the composition).

A - ref from S. Report

	Strontium Chloride	*Cresol(s)*
1. solution for applying externally and administration through the mouth.	6%	1% of *p*-cresol
2. solution for injections	10%	1% of *p*-cresol
3. eye ointment	20%	2.5% of a mixture *o*-, *m*- and *p*-cresol.
4. ointment for the treatment of contusions	20%	6% of a mixture of *o*-, *m* and *p*-cresol.
5. face cream	20%	4% of *p*-cresol
6. hair lotion	7%	6% of *o*-cresol
7. toothpaste	20%	4% of *p* cresol.

Laboratory investigations and clinical tests on the compositions in accordance with the invention gave the following results.

Laboratory investigations.

Two forms of the composition in accordance with the invention were used, namely (a) an aqueous solution containing 10% by weight strontium chloride and 1% by weight of *p*-cresol, and (b) an ointment containing 20% by weight strontium chloride and 2.5% by weight of a mixture of *o*-, *m*- and *p*-cresols.

The solution (a) injected into guinea pigs in dosages of 5 c.c. both subcutaneously and to a greater depth and also as an endodermic perfusion did not produce any inflammatory reactions. Daily subcutaneous injections of 10 c.c. of the solution (a) (one grm. of strontium chloride into rabbits for fifteen days did not produce any change in the basic functions and organs of the rabbit. There was neither irritation nor shock nor any circulation trouble as shown by E.C.G. There was no albuminurea nor bile constituents. There was no change of the skin hair and no change in the eyes. The kidneys and liver macroscopically and histologically were normal. The suprarenal glands were normal in appearance and so were the ovaries.

Intravenous injections of the solution (a) into rabbits and in the vein of the ear in dosages of 3 c.c. (initially) and dosages of 5 c.c. from the third day onwards, did not produce any disorganisation of the body functions and there was no change in the white and red blood corpuscles, nor was there any haemolysis.

In the case of experimental burns produced by endodermic injections of 0.5% quinine Hydrochloride there was very quick healing when the ointment (b) was applied compared with the time taken for the burns to heal when petroleum jelly was applied by itself.

Experiments were also carried out on frog's heart after removal of the pericardium, using instillations of the solution (a). There was no change of the rhythm and quality of the miocardian contractions.

The injection of 4 c.c. of the solution (a) into all the lymphatic spaces of the frog "ranafusca" did not produce any E.C.G. changes.

II. Clinical Tests.

1. *Mastitis.* In cases of mastitis i/v injections of solution (a) were given intraveneously for two days. There was quick relief from the inflammatory oedema and no suppuration occurred.

2. *Acute Tonsilitis.* Improvement in five cases was shown by injections of solution (a) as indicated by diminution of the oedema and fall of the temperature to normal levels.

3. *Rizitis and Sciaticae.* Improvements were obtained in four patients who had previously been found to be resistant to the normal methods of therapy. The pain almost subsided in four to give days following two daily intramuscular injections of solution (a). One of the cases was of one year's standing.

4. *Pleuritis.* Three were exudative. There was very rapid absorption of fluid on administration of injections of solution (a).

5. *Chronic Bronchitis.* Resistant to antibiotics. This was a case of a student suffering from chronic bronchitis. The culture of the bronchial discharge yielded the growth of Streptococcus and Staphyloccocus aureus resistant to all antibiotics. There was complete cure obtained by the use of 10 i/v injections of a solution (a).

An old man was relieved of his weekly remissions of fever by two daily i/v injections of solution (a) given for 14 days.

6. *Parotitis.* Five cases of parotitis with high temperatures were treated with i/v injections of solution (a) twice daily and there was quick relief from the oedema and fever in 3 to 4 days.

7. *Chronic Rheumatic Fever.* A case resistant to cortisone and heat therapy was successfully treated with i/v injections of solution (a).

8. *Varicose Ulcers and Bedsores.* There was considerable improvement of three varicose ulcers from the second day onwards of application of the ointment (b). In 10 cases of bedsores, healing was rapid.

9. *Eczema.* There was quick and obvious improvement in 6 cases of eczema after using the ointment (b). There was also quick relief from itching.

WHAT I CLAIM IS:—

1. A pharmaceutical composition for external and internal use comprising strontium chloride and one or more of *o*-cresol, *m*-cresol and *p*-cresol, and a pharmaceutically acceptable carrier therefore.

2. A pharmaceutical composition according to claim 1 comprising an aqueous solution of strontium chloride and one or more of *o*-cresol, *m*-cresol and *p*-cresol.

3. A pharmaceutical composition according to claim 1 or claim 2 and containing between 6 and 20% by weight strontium chloride and between 1 and 6% by weight of one or more of *o*-cresol, *m*-cresol and *p*-cresol.

4. A pharmaceutical composition according to claim 1 for external and internal use comprising an aqueous solution containing 6% by weight of strontium chloride and 1% by weight of *p*-cresol.

5. A pharmaceutical composition according to claim 1 for injections comprising an aqueous solution containing 10% by weight strontium chloride and about 1% by weight of *p*-cresol.

6. A pharmaceutical composition according to claim 1 in the form of an eye ointment containing 20% by weight of strontium chloride and 2.5% by weight of a mixture of *o*-, *m*-, and *p*-cresols.

7. A pharmaceutical composition according to claim 1 in the form of an ointment for external applications containing 20% by weight of strontium chloride and 6% by weight of a mixture of *o*-, *m*- and *p*-cresols.

8. A pharmaceutical composition according to claim 1 in the form of a cream containing 20% by weight of strontium chloride and 4% by weight of *p*-cresol.

9. A pharmaceutical composition according to claim 1 in the form of a hair lotion containing 7% by weight of strontium chloride and 6% by weight of *o*-cresol.

10. A pharmaceutical composition according to claim 1 in the form of a toothpaste containing 20% by weight strontium chloride and 4% by weight of *p*-cresol.

11. A method of preparing a pharmaceutical composition according to any preceding claim comprising forming an aqueous solution containing strontium chloride and one or more of *o*- *m*- and *p*-cresol and thereafter if desired, diluting with water or mixing the solution with one or more further pharmaceutically acceptable carriers.

12. A pharmaceutical composition according to claim 1 substantially as hereinbefore described.

13. A pharmaceutical composition whenever prepared by a method according to claim 11.

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